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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JENNIFER JONES MCINTIRE, ROSEMARIE DEKRUYFF,
DALE T. UMETSU, and GORDON FREEMAN

Appeal 2010-001105
Application 10/663,497
Technology Center 1600

Decided: June 18, 2010

Before DEMETRA J. MILLS, FRANCISCO C. PRATS,
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for lack of enablement and lack of written description. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF CASE

The following claims are representative.

1. A method of screening for a human individual's predisposition to atopy, the method comprising:

analyzing said individual for the presence of at least one TIM-1[1] polymorphism by contacting a biological sample comprising DNA or mRNA from said individual with probes that specifically bind under stringent conditions to nucleic acid sequences of a TIM-1 gene;

wherein the presence of said polymorphism is indicative of an individual's predisposition to develop said atopy.

4. The method according to Claim 1, wherein said analyzing step comprises

contacting a biological sample comprising DNA or mRNA from said individual with a probe that specifically binds to the nucleic acid sequence ATGACAACGACTGTTCCA, SEQ ID NO:22, BASES 472-489, encoding the amino acid sequence MTTTVP, SEQ ID NO:25, residues 158-163; and

detecting the presence of a complex formed between said probe and said DNA or mRNA.

7. The method according to Claim 1, wherein said biological sample is blood or a derivative thereof.

8. A method of screening for a human individual's predisposition to atopy, the method comprising:

analyzing said individual for the presence of an INS157 polymorphism in TIM-1 by contacting a biological sample comprising DNA or mRNA from such individual with a probe that specifically binds to the nucleic acid sequence ATGACAACGACTGTTCCA, SEQ ID NO:22, bases 472-489, encoding the amino acid sequence MTTTVP, SEQ ID NO:25, residues 158-163;

detecting the presence of a complex formed between said probe and said genomic DNA, mRNA or a transcript thereof; and

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[1] T-cell immunoglobulin domain and mucin domain.

analyzing said individual for the presence of hepatitis A virus (HAV) seropositivity wherein said seropositivity in an individual comprising an allele of TIM-I comprising the amino acid sequence MTTTVP, SEQ ID NO:25, residues 158-163 is indicative of a reduced risk of developing atopy.

20. A method of screening for a human individual's predisposition to atopy, the method comprising:

analyzing said individual for the presence of an INS1 57 polymorphism in TIM-1 by contacting a biological sample comprising DNA or mRNA from said individual with a probe that specifically binds to a nucleic acid sequence encoding the amino acid sequence MTTTVP, SEQ ID NO:25, residues 158-163;

wherein the presence of said INS157 polymorphism is indicative of an individual's predisposition to develop said atopy.

21. The method according to Claim 20, wherein said biological sample is blood or a derivative thereof.

22. The method according to Claim 20, further comprising the step of:

analyzing said individual for the presence of hepatitis A virus (HAV) seropositivity,

wherein seropositivity in an individual expressing an allele of TIM-1 comprising the amino acid sequence MTTTVP, SEQ ID NO:25, residues 158-163 is indicative of a reduced risk of developing atopy.

23. A method of screening for a human individual's predisposition to atopy, the method comprising:

analyzing said individual for the presence of at least one TIM-1 polymorphism in exon 3 by contacting a biological sample comprising DNA or mRNA from said individual with probes that specifically bind under stringent conditions to nucleic acid sequences in exon 3 of a TIM-I gene;

wherein the presence of said polymorphism is indicative of an individual's predisposition to develop said atopy.

Cited References

Kroese et al., *Genetic tests and their evaluation: Can we answer the key questions?*, 6 GENET MED 475-480 (2004).

Jack Lucentini, *Gene Association Studies Typically Wrong*, 18 THE SCIENTIST 20 (2004).

John P.A. Ioannidis,*Why Most Published Research Findings are False*, 2 PLoS MED e124 (2005).

Andrew T. Hattersley and Mark I. McCathy, *What makes a good genetic association study?* 366 LANCET 1315-1323 (2005).

Robert A. Hegele, *SNP Judgments and Freedom of Association*, 22 ARTH. THROMB. VASC. BIOL 1058-1061 (2002).

GeneCard, HAVCR1, hepatitis A virus cellular receptor, available at www.genecards.org pp. 1-11.

Noguchi et al., *Insertion/deletion coding polymorphisms in hHAVcr-1 are not associated with atopic asthma in the Japanese population*, 4 GENES AND IMMUNITY 170-173 (2003).

Dale T. Umetsu and Rosemarie H. DeKruyff, *Regulation of Tolerance in the Respiratory Tract TIM-1, Hygiene, and the Environment*, 1029 ANN. N.Y. ACAD. SCI. 88-93 (2004).

Graves et al., *Association of atopy and eczema with polymorphisms in T-cell immunoglobulin domain and mucin domain – IL-2-inducible T-cell kinase gene cluster in chromosome 5q33*, 118 J. ALLERG. CLIN. IMMUNOL 650-656 (2005).

McIntire et al., *Hepatitis A virus link to atopic disease*, 425 NATURE 576 (2003).

Sizing et al., *Epitope-Dependent Effect of Anti-Murine TIM-1 Monoclonal Antibodies on T Cell Activity and Lung Immune Responses*, 178 J. IMMUNOLOGY 2249-2261 (2007).

Chae et al., *Molecular Variations in the Promoter and Coding Regions of Human Tim-1 Gene and Their Association in Koreans With Asthma*, 64 HUMAN IMMUNOLOGY 1177-1182 (2003).

Gao et al., *Genetic variants of the T-cell immunoglobulin mucin 1 but not the T-cell immunoglobulin mucin 3 gene are associated with asthma in an African American population*, 115 J. ALLERGY CLIN. IMMUNOL. 982-988 (2005).

Grounds of Rejection

1. Claims l, 4, 7-8, and 20-23 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.
2. Claims 1, 4, 7, and 23 are rejected 35 U.S.C. § 112, first paragraph for lack of written description.

Discussion

ISSUE

The Examiner concludes that

> because the specification while being enabling for a method for determining a Caucasian or Asian's predisposition to atopy[2] protection by detecting the presence of homozygous polymorphism of 157insMTTTVP (polymorphism 1, SEQ ID No. 22), of TIM-1 in a hepatitis virus A positive Caucasian individual, wherein the presence of the MTTTVP insertion is indicative of a Caucasian's predisposition to protect against atopy, does not reasonably provide enablement for a method for screening for a human individual's predisposition to any atopy by analyzing for the presence of any TIM-1 polymorphism.

(Ans. 3.)

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[2] Atopy is defined as asthma, allergic rhinitis and atopic dermatitis according to the Specification, page 1.

Appellants contend that the Specification enables claims of the pending claim scope. Appellants contend that a description of common polymorphisms in TIM-1 and linkage of TIM-1 locus to the development of atopy can be found in the Specification on pages 8 and 13. (App. Br. 8.)

The issue is: Is the full scope of the claims supported by an enabling disclosure? More particularly, does the Specification enable a method for screening any form of atopy with any polymorphism of TIM-1, as claimed?

FINDINGS OF FACT

For a complete fact finding with respect to the lack of enablement rejection see the Answer pages 3-14.

PRINCIPLES OF LAW

> [A]s part of the *quid pro quo* of the patent bargain, the applicant's specification must enable one of ordinary skill in the art to practice the full scope of the claimed invention. That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art.

AK Steel Corp. v. Sollac, 344 F.3d 1234, 1244 (Fed. Cir. 2003) (citation omitted).

Factors that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *See In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

"Enablement is determined as of the effective filing date of the patent, *In re Hogan*, 559 F.2d 595, 604 (CCPA 1977)." *Plant Genetic Systems, N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339 (Fed. Cir. 2003). *See also Enzo Biochem Inc. v. Calgene Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999).

A claim may… encompass inoperative embodiments and still meet the enablement requirement of 35 U.S.C. § 112, first paragraph. *See Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984), *In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976).

ANALYSIS

We agree with the Examiner's statement of the enablement rejection as applicable to claims 1, 4, 7, and 23 and the Examiner's fact finding and responses to Appellants' argument and adopt them as our own. The Examiner has faithfully considered the *Wands* factors in the enablement analysis. We concur with these findings.

We do not find, however, that the Examiner's evidence supports lack of enablement of claims 8, 20, 21, and 22, particularly in view of the fact that the Examiner has indicated that the Specification is enabling for a method for determining a Caucasian or Asian's predisposition to atopy protection by detecting the presence of homozygous polymorphism of 157insMTTTVP (polymorphism 1, SEQ ID No. 22), of TIM-1 in a hepatitis

virus A positive Caucasian individual, and this is essentially the scope of claims 8 and 22. (Spec. ¶06; Ans. 3.)[3]

The fact that claims 8 and 22 also encompass other ethnic groups than Caucasian or Asian does not necessarily render these claims lacking in enablement. A claim may encompass inoperative embodiments and still meet the enablement requirement of 35 U.S.C. § 112, first paragraph. The Examiner has failed to show by a preponderance of the evidence that the one of ordinary skill in the art would have considered the majority of the claim scope as lacking in enablement.

With claims the scope of claims 8 and 22 enabled, it follows from the Specification and claims 8 and 22 that the presence of the INS157 polymorphism is indicative of an individual's predisposition to develop atopy and in claims 20 and 21. We find no evidence available at the time of filing of the present application to support lack of enablement of claims 20 and 21. The lack of enablement rejection with respect to claims 8 and 20-22 is reversed. The lack of enablement rejection of claims 1, 4, 7 and 23 is affirmed.

Written Description

Claims 1, 4, 7, and 23 are rejected 35 U.S.C. § 112, first paragraph for lack of written description.

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[3] While we understand that enablement and written description are separate statutory requirements we find it noteworthy that the Examiner has also considered claims 8, 20, 21, and 22 as described in the Specification as well, and has not included them in the written description rejection.

ISSUE

The Examiner finds that the Specification demonstrates that Appellants were in possession of a method for determining a Caucasian or Asian's predisposition to atopy protection by detecting the presence of homozygous polymorphism of 157insMTTTVP (polymorphism 1, SEQ ID No. 22), of TIM-1 in a hepatitis virus A positive Caucasian individual, wherein the presence of the MTTTVP insertion is indicative of a Caucasian's predisposition to protect against atopy.

Appellants contend that one of ordinary skill in the art would recognize a reasonable correlation between atopy and members of the genus is readily established by the disclosure of the instant application and since every species in the genus does not have to be tested for the genus to be enabled. (App. Br. 29.)

Issue: Does the written description support the pending claim scope? Were Appellants in possession of the pending claim scope?

PRINCIPLES OF LAW

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003).

The written description requirement applies to all claims and requires that the specification objectively demonstrate that the applicant actually invented—was in possession of—the claimed subject matter. *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d. 1336, 1349 (Fed. Cir. 2010). "Although many original claims will satisfy the written description requirement, certain claims may not. For example, a generic claim may

define the boundaries of a vast genus of chemical compounds, and yet the questions may still remain whether the specification, including the original claim language, demonstrates that the applicant has invention species sufficient to support a claim to the genus." *Id.* at 1370-1371. A sufficient description of a genus requires the disclosure of either a representative number of species falling within the scope of the genus, or structural features common to the members of the genus so that one of skill in the art can "visualize or recognize" the members of the genus. *Id.* at 1350.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997).

ANALYSIS

We concur with the Examiner's findings and conclusions with respect to the lack of written description rejection and pages 15-18 of the Answer. As to claim 1, the Examiner finds that the claimed invention

> encompasses methods comprising the analysis and detection of an enormous and wide variety of nucleic acid sequences. The claims are broadly drawn to a method that encompass a plurality of nucleic acids an extremely large genus of polymorphic variants of the TIM-1 gene with any nucleotide content (A or G or C or T) at any position within the TIM-1 gene. Thus the claims encompass the detection of any of different nucleic acids wherein the nucleic acid sequence is correlated with an association of disease. Nucleic acids of such a large genus have not been taught by the specification.
>
> In analyzing whether the written description requirement is met for genus claims, it is first determined whether a

> representative number of species have been described by their complete structure. The instant specification provides the sequence of SEQ ID No. 18, 20, 22, 24, 26, and 28. The specification also provides the amino acid sequence of TIM-1 as SEQ ID No. 19, 21, 23, 25, 27, and 29. The specification provides analysis of the insertion of the … amino acid sequence of MTTTVP at position 157 and indicating that this insertion is indicative of association of disease.

(Ans. 16.)

We conclude, as did the Examiner, that the "specification does not teach any association with any other polymorphic variation disclosed in the specification, for example deletion 195ΔThr, 157insMTTVP, T140A, V161A, V167I, T172A, and N258D that are indicative of association of atopic immunological disorders." (*Id.*)

To satisfy the written description requirement we determine whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence, gene name, and specific polymorphic position), specific features and functional attributes that would distinguish different members of the claimed genus. In the present case, the Specification does not provide any characteristics that would allow one to identify any other TIM-1 family of genes from another organism or any other particular polymorphisms, portions or fragments or variants of the disclosed sequence that would allow for the diagnosis of any type of atopic immunological disorder based on detection of the non-disclosed gene. (Ans. 16-17.)

The Specification supports that the inventor was in possession the claimed method of screening to the extent that the insertion of the amino acid sequence MTTTVP at position 157 and indicates that this insertion is

indicative of association of disease and that persons with this insert, who are hepatitis A positive have a predisposition toward protection against atopy. We do not find the Specification provides a description of any other polymorphism associated with atopy in a manner which evidences possession of the genus of TIM-1 polymorphisms generally.

In sum we find no evidence of record of a representative number of polymorphisms associated or used to determine a predisposition to atopy to indicate that the inventor was in possession of the invention throughout the full claim scope of claim 1.

CONCLUSION OF LAW

The enablement rejection is affirmed as to claims 1 4, 7, and 23, but reversed as to claims 8, and 20-22. The written description rejection is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

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